UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FIL	ATTORNEY DOCKET NO.
09/045,732	03/20	233/127

T NAMED INVENTOR	EXAMINER
C	SIU,S

ART UNIT	PAPER NUMBER
1631	9

MAILED: 05/03/00

022249
LYON & LYON LLP
SUITE 4700
633 WEST FIFTH STREET
LOS ANGELES CA 90071-2066

Please find below and/or attached an Office communication concerning this applica... proceeding.

Commissioner of Patents and Trademar...

1- File Cop

US GPO 1999 460-693

PTO-90C (Rev 2/95

Office Action Summary	Application No. 09/045,732	Applicant(s) FULLER ET AL.	
	Examiner Stephen C Siu	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on April 7, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/045,732 is acceptable and a CPA has been established. An action on the CPA follows.

Specification

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Revision of the content of the abstract is required on a separate sheet.

Claim Objections

Claims 10, 12, 16, 18 are objected to because of the following informalities: Claim 10 describes the compound "deoxyguonosine" and claim 12 describes the compound "deoxyguanisine". Both terms appear to be misspelled. Claim 16 duplicates the word "is" and claim 18 duplicates the word "wherein". Appropriate correction is required.

Double Patenting

Applicant is advised that should claims 5 and 6 be found allowable, claims 17 and 18, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. "Propyl-7-deaza-2'-deoxyguanosine" in Claim 11 is not described in the specification which instead describes "7-propyl-7-deaza-2'-deoxyguanosine".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-11, 13, 15-16, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) teaches on page 7 a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the instant invention. The R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III in which the R5 group of analog II described by Gilead Sciences is H, lower alkyl (1-4C), CN, Br, Cl, F, CONR2, lower alkenyl (1-4C) or lower alkynyl (1-4C). The R1 group of the molecule of formula II recited in the claimed molecule is a C_{1-10} alkyl group optionally substituted by hydroxyl, amino, C_{1-4} alkoxy or halo as recited in Claim 1, for example. Likewise, the R3 group of the molecule of formula III is a C_{2-10} alkynyl group as recited in Claim 19, for example. Analog II disclosed by Gilead Sciences, Inc. anticipates the molecule of formula II in the present invention as, for example, a C_4 alkyl substituted as R5 in analog II would anticipate such a molecule with a like alkyl substituted for R1 in the molecule of formula II or a C4 alkynyl substituted as R3 in the molecule of formula III in the present invention. Furthermore, analog II disclosed by Gilead Sciences encompasses the claimed molecules of both claim 10 and 11 in the present invention, R5 being an ethyl group or propyl group, respectively. Also, Gilead Sciences discloses the incorporation of analogs

of structural formula II, wherein R5 is hereinbefore described, into oligomers designed for triple-helix formation with a comlementary duplex DNA strand thus anticipating claim 16 in which the base of the same structure as that described by Gilead is used in a deoxyribonucleic acid sequence. Further, the oligonucleotides or oligomers of Gilead include DNA or RNA (page 10, lines 14-21).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-13, 15-16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93) in view of Li (Nucleic Acids Research, 1993, Vol.21, Nol.11, pages 2709-2714) and in further view of Seela and Thomas (Helvetica Chimica Acta, Feb 22, 1995, Vol.78, pages 94-108).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the claimed invention wherein the R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III. The R5 group of analog II described by Gilead Sciences is

H, lower alkyl (1-4C), CN, Br, Cl, F, CONR2, lower alkenyl (1-4C) or lower alkynyl (1-4C).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) does not disclose the molecule wherein the R5 group is a higher alkyl C(5-10).

Li (Nucleic Acids Research, 1993, Vol.21, Nol.11, pages 2709-2714) discloses a method of resolving band compression on electrophoretic bands by substituting a purine base with an analog and destabilization of the oligonucleotide. Li discloses improvement in band compression would be accomplished by substituting with N4-methyl-dCTP and teaches prior studies done using 7-deaza-dGTP analogs. Li also suggested the use of more bulky alkyl groups.

Li does not further disclose additional substitutions on purine or pyrimidine bases.

Seela and Thomas (Helvetica Chimica Acta, Feb 22, 1995, Vol.78, pages 94-108) disclose a method of stabilization of DNA through substitutions on pyrimidine bases with methyl groups. Seela and Thomas state that small pyrimidine 5-substituents have steric freedom in the major groove of B-DNA but that if their size is increased, then structural changes occur to decrease the Tm and hence their stability. Seela and Thomas further teach a similar situation in 7-substituted 7-deazapurines.

One of ordinary skill in the art would have been motivated to utilize a substituent larger than a methyl group on a 7-substituted 7-deazapurine because the compound previously disclosed by Gilead Sciences uses a C(1-4) substituent while Li taught the

substitution of a methyl group in the resolution of compression artifact on electrophoretic gels while suggesting the use of larger groups despite potential problems with false stops. Further, as per teachings of Seela and Thomas, oligonucleotide stability is decreased with substitutions on pyrimidine bases with methyl groups and if the size of the pyrimidine substituents is increased then steric freedom in the major groove of B-DNA is hindered and stability would decrease. Seela and Thomas also stated that this principle is applicable to 7-substituted 7-deazapurines. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, motivated by resolving band compression of electrophoretic bands, to perform the teachings of Li on the analog of Gilead Sciences by substitution of bases and substituting larger groups on 7-substituted 7-deazapurines to increase instability thereby improving resolution of band compression of electrophoretic bands of the oligonucleotide as per the teachings of Seela and Thomas.

Claim 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE), Inc in view of Stryer (Biochemistry, 3rd Ed., 1988, W.H. Freeman & Col, New York)

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule for incorporation into oligomers as described above.

Gilead Sciences does not demonstrate the use of the nucleoside/nucleotide molecule in a method for determining the nucleotide base sequence of a DNA molecule.

Stryer discloses methods of DNA sequencing using nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the nucleotide analog of Gilead Sciences in DNA sequencing because DNA sequencing was demonstrated to be successful with nucleotides through the teachings of Stryer. One of ordinary skill in the art would therefore have been motivated to apply known DNA sequencing techniques to the nucleotide analog of Gilead Sciences with a reasonable expectation of success.

Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) in view of Mathews, Christopher; Biochemistry, Benjamin/Cummings Publishing Company, Inc., 1990.

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule and the incorporation of the molecules into oligomers as described above.

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) does not demonstrate the method of elongation of an oligonucleotide sequence (incorporation of molecules into oligomers).

Mathews discloses the method of polynucleotide chain elongation with DNA polymerase and nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the nucleotide of Gilead Sciences in the elongation of an oligonucleotide sequence because Gilead Sciences demonstrates the incorporation of the nucleotide molecules into oligomers and Mathews provides the means in which incorporation of the nucleotide molecules into oligomers would be accomplished successfully. The base analog was known in the art through the teachings of Gilead Sciences who also taught the incorporation of the analogs into polynucleotides. Chain elongation procedures were demonstrated to be successful in incorporation of nucleotides into oligomers through the teachings of Mathews. Thus, one of ordinary skill in the art would have been motivated through the combined teachings of Gilead Sciences and Mathews to incorporate the nucleotide analogs of Gilead Sciences into oligomers by utilizing chain elongation procedures of Mathews with a reasonable expectation of success.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) in view of Carey, Francis A., Organic Chemistry, 2nd Edition, McGraw Hill, 1992 .

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule for incorporation into oligomers designed for

triple-helix formation with a complementary duplex DNA strand wherein R5, corresponding to R1 in the claimed molecule (II) and R3 in the claimed molecule (III), is a C_{1-4} alkyl or C_{2-10} alkynyl group, respectively. Gilead Sciences further discloses a synthesis method for said molecule using a "suitably protected nucleotide" (page 22, line 6 and 15).

Gilead Sciences does not disclose the distinct process for the preparation of the molecule (II).

Carey discloses the concepts of protection groups and reduction in the synthesis of organic compounds.

One of ordinary skill in the art would have been motivated to apply organic chemistry principles as set forth by Cary to synthesize molecule II disclosed by Gilead Sciences wherein R5 is a lower alkyl (1-4C) from molecule II disclosed by Gilead Sciences wherein R5 is a lower alkynyl (1-4C) because the molecule was known in the art through the teachings of Gilead Sciences and synthesis steps were also known in the art through the teachings of Carey. It would have been obvious to one of ordinary skill in the art at the time the invention was made to rely on the synthesis methods set forth by Carey to synthesize the molecule of Gilead Sciences with a reasonable expectation of success.

Conclusion

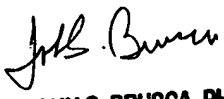
No claims allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stephen Siu, whose telephone number is (703) 308-7522. The Examiner can normally be reached from 7:00 a.m. to 3:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028. Papers related to this application may be submitted to Art Unit 1631 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 308-0294. Please call the Examiner at (703) 308-7522 before the transmission to expedite delivery of the fax. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephen Siu

04/28/00



JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER